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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,762	10/12/2001	Margaret Shipp	DFN-031US	2130

959 7590 04/07/2004

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EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/830,762	SHIPP ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): see attached.

4. ☒ Newly proposed or amended claim(s) *1, 2, 25-28* would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☒ The drawing correction filed on *03 March 2004* is a)☒ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

The rejection of claims 1, 2 and 25-28 under 35 U.S.C. 112, **is withdrawn** in view of Applicant's amendments to the claims.

The rejection of claims 4-10, 20 and 29-31 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising SEQ ID NO. 2 encoded by the nucleic acid sequence set forth in SEQ ID NO: 1 or 3, does not reasonably provide enablement for an isolated polypeptide or an isolated nucleic acid molecule that is at least 90% of 95% homologues to SEQ ID NO: 1, 2 or 3 **is maintained** for reasons of record.

Applicant's arguments and the examiners rebuttal are essentially the same of record. Applicant's arguments are that procedures for making variants of a nucleic acid sequence are conventional in the art especially when coupled to a catalytic activity. In this instance Applicant's arguments are that the new limitation "wherein elevated levels of said nucleic acid molecules are indicative of a malignancy", is the same as claiming a catalytic function. Applicants arguments are that the specification teaches that only conservative substitutions of one or more amino acids of SEQ ID NO: 2 or 5, deletion or insertion of non-critical in non critical region of the protein. The specification does not set for the what specific structures are non-critical to the function of ""wherein elevated levels of said nucleic acid molecules are indicative of a malignancy". Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any and all nucleic acid fragments with sequence similarity to the amino acid sequence shown in SEQ ID NO. 2. Therefore, in view of the speculative nature of the invention, the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as

claimed, which include variation in the nucleic acid sequence resulting in changes in the encoded protein sequence.

The rejection of claims 1, 2 and 25-28 under 35 U.S.C. 112, **is withdrawn** in view of Applicant's amendments to the claims.

The rejection of claims 4-10, 20 and 29-31 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention **is maintained** for reasons of record. The written description in this case only sets forth SEQ ID NO: 1, 2 and 3 and therefore the written description is not commensurate in scope with claims that read on 90%-95 % sequence homology to SEQ ID NO. 2.

Applicant's arguments and the examiners rebuttal are essentially the same of record. Applicant's argue that the new limitation "wherein elevated levels of said nucleic acid molecules are indicative of a malignancy" is a sufficient catalytic activity that allows the ordinary artisan to predictably make the contemplated variants. Applicant's cite the interim written description guidelines. No disclosure, beyond the mere mention of biologically active fragments is made in the specification. With the exception of nucleic acids encoding SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and/or encoded variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention

and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. The limitation "wherein elevated levels of said nucleic acid molecules are indicative of a malignancy" does not provide predictable/repeatable means of measuring a structure function relationship. Therefore, only a nucleic acid sequence of SEQ ID No: 1 or 3 encoding the polypeptide sequence of SEQ ID NO. 2 meets the written description provision of 35 USC 112, first paragraph.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

The official fax phone number for the organization where this application or proceeding is assigned is 703-872-9306; for informal communications please the fax phone number is 571-273-0912.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 9/5/04